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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,825	03/30/2001	Fiona Duffner	10018.200-US	6134

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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/823,825	DUFFNER ET AL.	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,15,19-21,29,30 and 39-48* is/are pending in the application.

4a) Of the above claim(s) *40-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,15,19-21,29,30 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment and the response filed on 3/8/04 has been fully considered and entered into the application.

2. Claims 1-2, 4, 15, 19-21, 29-30, 39-48 are currently pending in this application.

3. Claims 40-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. filed on 2/26/03.

4. This application contains claims 40-48 are drawn to an invention nonelected without traverse in Paper filed on 2/26/03. A complete reply to the final rejection must include cancellation of nonelected claims.

5. Claims 3, 5-14, 16-18, 22-28, and 31-38 have been canceled. Claim 1 has been amended. Claims 1-2, 4, 15, 19-21, 29-30, 39 are currently being examined in this application.

6. The indefinite-ness rejections and art rejections of record have been withdrawn in view of the amendments to the claims.

New Claim Rejections Necessitated by the Amendment

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-2, 4, 15, 19-21, 29-30 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite by reciting 'isolating the complete sequence of the

gene...', it is not clear what does applicants mean by complete sequence. Applicants are requested to clarify.

Claim 1 recites the limitation "the complete sequence". There is insufficient antecedent basis for this limitation in the claim.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: The instant claimed method is drawn to a method for identifying and isolating a gene of interest from a gene library... comprising: a) providing a genomic DNA library or cDNA library; b) inserting into said library a DNA fragment comprising a transposon and a ..... polynucleotide encoding a secretion reporter; c) introducing the library comprising the inserted DNA fragment into a host cell; d) screening for and selecting a host cell that secretes are partially secretes the active secretion reporter; e) identifying the gene of interest into which the secretion reporter was inserted in the selected host cell, by sequencing the DNA flanking the inserted DNA fragment....'. From the claimed method steps it is not clear how the gene of interest is related to the DNA fragment comprising the secretion reporter. Does applicants mean in step a) the genomic DNA library or cDNA library comprises the gene of interest or the secretion reporter protein is encoded by the gene of interest. And further if the cDNA library comprises the gene of interest, it is not clear how the complete sequence of the gene of interest is determined.

Claim 30 recites the limitation "the complete gene of interest". There is insufficient antecedent basis for this limitation in the claim or in claim 1.

Claim 39 recites the limitation "the complete gene of interest". There is insufficient antecedent basis for this limitation in the claim or in claim 1.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-2, 4, 15, 19-21, 29-30 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/22491 (McCarthy et al) and US Patent 5,948,622 (REZNIKOFF et al).

The instant claimed method briefly recites a method for identifying and isolating a gene of interest from a gene library, comprising: a) providing a genomic DNA library of cDNA library; b) inserting into said library a DNA fragment comprising a transposon and a promotorless and signal-less poynucleotide encoding a secretion reporter, wherein said inserting of said DNA fragment into said library is by in vitro transposition; c) introducing the library comprising the inserted DNA fragment into a host cell; d) screening for and selecting a host cell

that secretes or partially secretes the active secretion reporter; e) identifying the gene of interest into which the secretion reporter was inserted in the selected host cell; and f) isolating the complete sequence of the gene of interest in step e).

(NOTE that the gene of interest is the 'secretary protein').

McCarthy et al teach a method for identifying a cDNA encoding a mammalian protein having a signal sequence (refers to the gene of interest which encodes a polypeptide carrying a signal sequence for secretion of the instant claims) (i.e., see the abstract). The reference method includes the following steps: a) providing a library of mammalian cDNA (refers to step a) of the instant claims); b) ligating the library of mammalian cDNA to DNA encoding alkaline phosphates lacking both a signal sequence and a membrane anchor sequence (refers to a DNA fragment comprising a promoter-less and secretion signal less polynucleotide encoding a secretion reporter of the instant claims) to form ligated DNA (refers to the step b of the instant claims); c) transforming bacterial cells (refers to host cells of the instant claims) ligated DNA (refers to the step c) of the instant claims); d) isolating DNA comprising mammalian cDNA ; e) transfecting DNA isolated from step d) into a mammalian cells which do not express alkaline phosphatase; g) identifying the clones in bacterial cell clone corresponding to the clone in mammalian cell clone library (refers to step d) of the instant claims); h) isolating and sequencing a portion of the mammalian cDNA present in the bacterial cell library clone identified in step g) to identify a mammalian cDNA encoding a mammalian protein having a signal sequence (refers to step f) of the instant claims) (i.e., see abstract). The reference teaches that using the method a purified DNA, which includes a sequence encoding a protein (ethb0018f2). McCarthy et al teach that the DNA sequence of ethb0018f2 revealed that the ethb0018f2 cDNA encodes a 467 amino

acid reading frame (refers to the complete gene of interest and the gene encodes a protein of the instant claims) (i.e., see page 17).

The claimed invention differs from the prior art teachings by reciting that a transposon and a promotor-less and secretion signal less secretary reporter into the library by in vitro transposition.

McCarthy et al do not teach the use of DNA fragment carrying a transposon along with the secretary reporter or in vitro transposition of the DNA fragment. However, Reznikoff et al teach a system for in vitro transposition that includes a donor DNA that includes a transposable element flanked by a pair of transposon, a target DNA into which the transposable element can transpose (e.g., see abstract). Reznikoff et al teach the disclosed method, employing the modified transposases described herein and a simple donor DNA is applicable to introduce changes into any target DNA, is broadly applicable to introduce changes into any target DNA, without regards its nucleotide sequence. The reference teaches in vitro transposition of donor DNA into a target DNA, and the transposition can be assayed by introducing the nucleic acid into a suitable host cells (refers to the genomic DNA or cDNA library of the interest) (refers to the inserting of said DNA into the library by in vitro transposition of the instant claims) (i.e., see column 5). McCarthy et al teach the transposable element can include any desired nucleotide sequence. The transposable element can include a coding region that encodes a detectable or secretable protein with or without associated regulatory elements such as promoter, terminator (refers to the 'promotorless and signal-less polynucleotide encoding secretary reporter' of the instant claims) or the like (i.e., see column 10). The reference teaches that the products generated by the in vitro transposition method can be used as templates in standard nucleic acid sequencing reactions to

reveal the nucleic acid sequences of the insert (i.e., see column 3). The reference teaches that the in vitro transposition method has efficiency, and can be broadly applied in various ways (i.e., see column 3).

Thus, it would have been obvious to one skilled in the art at the time the invention was made to use the in vitro transposition method taught by Reznikoff et al with the method for identifying a cDNA taught by McCarthy et al, because the Reznikoff et al teach the advantages of the use of the in vitro transposition method. A person skilled in the art would have been motivated to use the in vitro transposition method taught by Reznikoff et al with the McCarthy et al method, such that the nucleic acid sequence of the DNA can be determined with high efficiency.

13. Claims 1-2, 4, 15, 19-21, 29-30 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,150,098 (Zhang et al) and US Patent 5,948,622 (Reznikoff et al).

Zhang et al disclose methods for identifying novel secreted mammalian proteins in mammalian host cells. The invention provides a method for trapping signal sequence DNA from cDNA libraries and the cDNA libraries are constructed in a signal trap vector for transfection into a mammalian host cell and detecting secretion of reporter polypeptide. The signal trap vector contains DNA encoding a reporter polypeptide, which lacks a functional signal sequence. The reference method comprises the following steps: a) constructing a mammalian cDNA library (refers to step a) of the instant claims); b) inserting the cDNA library into a signal trap vector comprising DNA encoding a reporter polypeptide lacking a functional signal sequence; d) transfecting the library into a mammalian host cell lacking the functional reporter polypeptide (refers to step c) of the instant claims); e) selecting transfected mammalian cells (refers to step d)

of the instant claims); f) analyzing DNA recovered from the transfected cells (refers to step e) of the instant claims); g) screening a mammalian cDNA library to identify a full-length cDNA (i.e., see summary of the invention). The reference discloses that the secretion of reporter polypeptide may be determined by growth on selective medium requiring the presence of the secreted reporter polypeptide (refers to instant claim 19) (i.e., see column 4, lines 39-42). Zhang et al disclose that a cDNA library may also be screened for genes encoding full-length secreted polypeptides by PCT using primers based upon the sequences obtained by signal trapping (refers to instant claim step f, claims 29-30) (i.e., see column 10, lines 16-18).

The claimed invention differs from the prior art teachings by reciting that a transposon and a promotor-less and secretion signal less secretary reporter into the library by in vitro transposition.

Zhang et al do not teach the use of DNA fragment carrying a transposon along with the secretary reporter or in vitro transposition of the DNA fragment. However, Reznikoff et al teach a system for in vitro transposition that includes a donor DNA that includes a transposable element flanked by a pair of transposon, a target DNA into which the transposable element can transpose (e.g., see abstract). Reznikoff et al teach the disclosed method, employing the modified transposases described herein and a simple donor DNA is applicable to introduce changes into any target DNA, is broadly applicable to introduce changes into any target DNA, without regards its nucleotide sequence. The reference teaches in vitro transposition of donor DNA into a target DNA, and the transposition can be assayed by introducing the nucleic acid into a suitable host cells (refers to the genomic DNA or cDNA library of the interest) (refers to the inserting of said DNA into the library by in vitro transposition of the instant claims) (i.e., see column 5).

McCarthy et al teach the transposable element can include any desired nucleotide sequence. The transposable element can include a coding region that encodes a detectable or secretable protein with or without associated regulatory elements such as promoter, terminator (refers to the 'promotorless and signal-less polynucleotide encoding secretary reporter' of the instant claims) or the like (i.e., see column 10). The reference teaches that the products generated by the in vitro transposition method can be used as templates in standard nucleic acid sequencing reactions to reveal the nucleic acid sequences of the insert (i.e., see column 3). The reference teaches that the in vitro transposition method has efficiency, and can be broadly applied in various ways (i.e., see column 3).

Thus, it would have been obvious to one skilled in the art at the time the invention was made to use the in vitro transposition method taught by Reznikoff et al with the method for identifying a cDNA taught by Zhang et al, because the Reznikoff et al teach the advantages of the use of the in vitro transposition method, and Zhang et al teach that the cDNA library may also be screened for genes encoding full-length secreted polypeptides by PCR using primers based upon the sequences obtained by signal trapping. A person skilled in the art would have been motivated to use the in vitro transposition method taught by Reznikoff et al with the Zhang et al method, such that the complete nucleic acid sequence of the DNA can be determined with high efficiency.

14. Claims 1-2, 4, 15, 19-21, 29-30 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/40146 (Jacobs et al) and US Patent 5,948,622 (Reznikoff et al).

Jacobs et al teach yeast invertase gene as reporter system for isolating cytokines. The

reference method for isolating cDNA encoding a novel secreted mammalian protein includes the following method steps: a) constructing a cDNA library (refers to step a) of the instant claims); b) ligating cDNA library to a DNA encoding a non-secreted yeast invertase (refers to step b) of the instant claims); c) transforming the ligated DNA into E.coli (refers to step c) of the instant claims); d) isolating plasmid DNA containing mammalian cDNA ligated to the DNA encoding non secreted yeast invertase (refers to instant claim20); e) transforming the DNA of step d) into a yeast cell which does not contain the invertase gene; f) selecting yeast cells capable of growth on sucrose or raffinose (refers to step d) of the instant claims); g0 purifying DNA; h) screening the cDNA library to detect full length cDNAs which contain novel mammalian leader sequence; I) isolating the full length cDNA (refers to step f) of the instant claims) (i.e., see summary of the invention). The reference in page 11, teaches the novel secreted and extracellular proteins of the invention encoded by the mammalian cDNA (refers to complete gene of interest of the instant claims).

The claimed invention differs from the prior art teachings by reciting that a transposon and a promotor-less and secretion signal less secretary reporter into the library by in vitro transposition.

Jacobs et al do not teach the use of DNA fragment carrying a transposon along with the secretary reporter or in vitro transposition of the DNA fragment. However, Reznikoff et al teach a system for in vitro transposition that includes a donor DNA that includes a transposable element flanked by a pair of transposon, a target DNA into which the transposable element can transpose (e.g., see abstract). Reznikoff et al teach the disclosed method, employing the modified transposases described herein and a simple donor DNA is applicable to introduce changes into

any target DNA, is broadly applicable to introduce changes into any target DNA, without regards its nucleotide sequence. The reference teaches in vitro transposition of donor DNA into a target DNA, and the transposition can be assayed by introducing the nucleic acid into a suitable host cells (refers to the genomic DNA or cDNA library of the interest) (refers to the inserting of said DNA into the library by in vitro transposition of the instant claims) (i.e., see column 5). McCarthy et al teach the transposable element can include any desired nucleotide sequence. The transposable element can include a coding region that encodes a detectable or secretable protein with or without associated regulatory elements such as promoter, terminator (refers to the 'promotorless and signal-less polynucleotide encoding secretary reporter' of the instant claims) or the like (i.e., see column 10). The reference teaches that the products generated by the in vitro transposition method can be used as templates in standard nucleic acid sequencing reactions to reveal the nucleic acid sequences of the insert (i.e., see column 3). The reference teaches that the in vitro transposition method has efficiency, and can be broadly applied in various ways (i.e., see column 3).

Thus, it would have been obvious to one skilled in the art at the time the invention was made to use the in vitro transposition method taught by Reznikoff et al with the method for identifying a cDNA taught by Jacobs et al, because the Reznikoff et al teach the advantages of the use of the in vitro transposition method, and Jacobs et al teach that the cDNA library may also be screened for genes encoding full-length secreted polypeptides by PCR using primers based upon the sequences obtained by signal trapping. A person skilled in the art would have been motivated to use the in vitro transposition method taught by Reznikoff et al with the Jacobs

et al method, such that the complete nucleic acid sequence of the DNA can be determined with high efficiency.

Response to Arguments

16. Applicant's arguments with respect to amended claim 1-2, 4, 15, 19-21, 29-30 and 39 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

17. No claims are allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809.

The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

Pp
28 May 2004

PADMASHRI PONNALURI
PRIMARY EXAMINER